Attorney Docket No.: 6692.204-US PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Lau et al. Confirmation No.: 7549

Application No.: 10/572,348 Group Art Unit: 1654

Filed: March 17, 2006 Examiner: Ha, Julie

For: Novel GLP-1 Derivatives

RESPONSE TO RESTRICTION REQUIREMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This paper is being filed in response to the Office Action mailed October 17, 2008 that made restriction and election of species requirements. Applicants were requested to elect one of 49 designated groups:

> Group 1, claim(s) 76-123, 126-128, 138, and 140-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is GLP-1, hydrophilic spacer is -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.
>
> Group 2, claim(s) 76-111, 124, 128, 138 and 140-141, drawn to drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is exendin-4, hydrophilic spacer is -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.
>
> Group 3, claim(s) 76-111, 125, 128, 138 and 140-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is ZP-10 (i.e., HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPSKKKKKK-amide), hydrophilic spacer is -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.
>
> Group 4, claims 76-110, 129-132, 138, 140-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is GLP-2, hydrophilic spacer is -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 5, claims 76-110, 133-134, 138,140-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is human insulin, hydrophilic spacer is -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 6, claims 76-110, 135, 138, 140-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is human growth hormone or an analog thereof, hydrophilic spacer is -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 7, claims 76-110, 136, 138, 138, 140-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is parathyroid hormone or an analog thereof, hydrophilic spacer is -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 8, claims 76-110, 137, 138, 140-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is follicle stimulating hormone or an analog thereof, hydrophilic spacer is -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 9, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a growth factor, hydrophilic spacer is -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 10, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a somatomedin, hydrophilic spacer is -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 11, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a interferon, hydrophilic spacer is -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 12, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a pro-urokinase or urokinase, hydrophilic spacer is -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 13, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a tissue plasminogen activator (t-PA), hydrophilic spacer is -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 14, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a plasminogen activator inhibitor 1, hydrophilic spacer is -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 15, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a plasminogen activator inhibitor 2, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 16, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a von Willebrandt factor, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 17, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a cytokine, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 18, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a colony stimulating factor (CFS), hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 19, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a stem cell factor, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 20, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a tumor necrosis factor, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 21, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a protease inhibitor, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 22, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is an opioid, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 23, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a hormone, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 24, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a neuropeptide, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 25, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a melanocortin, hydrophilic spacer is -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 26, claims 142-143, drawn to a method of treating type 2 diabetes in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 27, claim 142, drawn to a method of treating hyperglycemia in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 28, claim 142, drawn to a method of treating impaired glucose tolerance in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 29, claim 142, drawn to a method of treating type 1 diabetes in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 30, claim 142, drawn to a method of treating obesity in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 31, claim 142, drawn to a method of treating hypertension in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 32, claim 142, drawn to a method of treating syndrome X in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 33, claim 142, drawn to a method of treating dyslipidemia in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 34, claim 142, drawn to a method of treating cognitive disorders in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 35, claim 142, drawn to a method of treating atheroschlerosis in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 36, claim 142, drawn to a method of treating myocardial infarction in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 37, claim 142, drawn to a method of treating coronary heart disease in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 38, claim 142, drawn to a method of treating stroke in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 39, claim 142, drawn to a method of treating inflammatory bowel syndrome in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 40, claim 142, drawn to a method of treating dyspepsia or gastric ulcer in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 41, claim 144, drawn to a method of decreasing food intake in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 43, claim 144, drawn to a method of increasing β-cell function and β-cell mass in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 44, claim 144, drawn to a method of restoring glucose sensitivity to β-cells in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 45, claim 145, drawn to a method of treating small bowel syndrome, inflammatory bowel syndrome or Crohns disease, said method comprising administering to a subject in need thereof an effective amount of a compound of GLP-2 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 46, claim 146, drawn to a method of treating hyperglycemia in a person in need thereof, comprising administering to said subject an effective amount of a compound of human insulin or an analog thereof and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

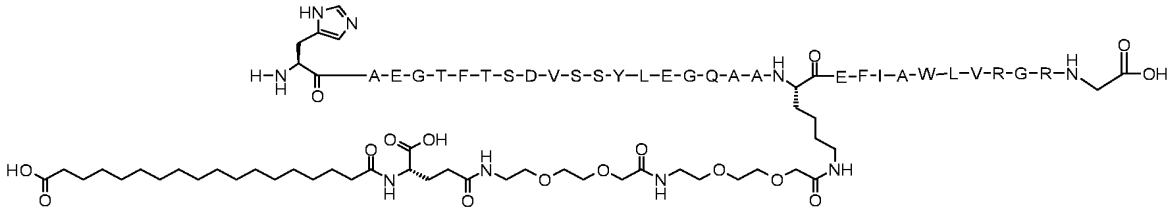
Group 47, claim 146, drawn to a method of treating type 1 diabetes in a person in need thereof, comprising administering to said subject an effective amount of a compound of human insulin or an analog thereof and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 48, claim 146, drawn to a method of treating type 2 diabetes in a person in need thereof, comprising administering to said subject an effective amount of a compound of human insulin or an analog thereof and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 49, claim 146, drawn to a method of treating β-cell deficiency in a person in need thereof, comprising administering to said subject an effective amount of a compound of human insulin or an analog thereof and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

In response to these requirements, Applicants hereby elect with traverse the invention of Group 1, claims 75-123, 126-128, 138 and 140-141, and the species of Example 61

$N^{\varepsilon 26}$-[2-(2-[2-(2-[2-(2-[4-(17-Carboxyheptadecanoylamino)-4(S)-carboxybutyrylamino]ethoxy)ethoxy]acetylamino)ethoxy]ethoxy)acetyl][Arg^{34}]GLP-1-(7-37)-OH



In addition, paragraph 8 of the Restriction Requirement required that if Group 1 was elected, Applicants should specify, in addition to the formula for the species (i.e. compound) elected within that group (which formula is shown above), what each variable is (Applicants assume the Examiner refers to the formulas of claim 76 and 77 and wants to know what the variables D, E, Q, W, B, Y etc. designates) and whether the GLP-1 polypeptide is DPP IV protected or the compound is DPP-IV stabilized. Accordingly, Applicants state that the compound of Example 61 is DPP-IV stabilized and the variables for this compound are as follows:

A is the penultimate formula on p. 14 of the application
W is -C(O)NH- (claim 84)
Y is -C(O)- (claim 83)
B is a hydrophilic spacer of claim 77 in which D=E= -O-; l=n=2; m=p=q=1 and
in Q: Z is -C(O)NH-, D=G=-O-, l=n=m=2, and p=0.

Claims 75-77, 83-92, 94-95, 100-105, 107, 109, 111-117, 118, 119, 121, 123, 128, 138 and 140-141 read on the elected species. Applicants hereby reserve the right to file continuing applications directed to the nonelected subject matter.

The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this response or application.

Respectfully submitted,

Date: February 17, 2009

/Richard W. Bork, Reg. No. 36,459/

Richard W. Bork, Reg. No. 36,459
Novo Nordisk Inc.
Customer Number 23650
(609) 987-5800

Use the following customer number for all correspondence regarding this application.

23650
PATENT TRADEMARK OFFICE